Studying the relationship between the CYP3A and CYP2D6 probe dextromethorphan and the pharmacokinetics of tamoxifen.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON24889

Source
NTR

Brief title
N/A

Health condition

relationship between the CYP3A and CYP2D6 probe dextromethorphan and the pharmacokinetics of tamoxifen in breast cancer patients who require tamoxifen monotherapy

Sponsors and support

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Intervention

Outcome measures

Primary outcome

Relationships between dextromethorphan clearance and the clearance of tamoxifen in breast cancer patients.

Secondary outcome

Relationships between other PK-parameters (AUC, Cmax and Tmax); effects of known polymorphisms in CYP2D6 and CYP3A and other relevant drug metabolizing enzymes and transporters on the pahrmacokinetics of tamoxifen and dextromethorphan.

Study description

Background summary

In this observational trial we would like to study the possible correlation between the probe-drug dextromethrophan and tamoxifen pharmacokinetics. In case a good correlation is available, this might help in a stepwise development of truly individualizing tamoxifen treatment. Study objectives are relationships between dextromethorphan clearance and the clearance of tamoxifen in breast cancer patients; relationships between other PK-parameters (AUC, Cmax and Tmax); effects of known polymorphisms in CYP2D6 and CYP3A and other relevant drug metabolizing enzymes and transporters on the pahrmacokinetics of tamoxifen and dextromethorphan. In one center (Erasmus Medical Center at Rotterdam, the netherlands), a total of 37 eligable patients, treated with a dose of 20 or 40 mg of tamoxifen, depending on their indication, will be given 30 mg dextromethorphan orally at day 1. Pharmacokinetic sampling will be performed at given time-points (pre, 30 min-24hours, in total 9 sampling time points). For dextromethorphan, blood samples will be processed to plasma and stored until analysis by a validated liquid chromatography tandem mass spectometry method. For tamoxifen, blood samples will be processed to serum and stored

until analysis by a validated liquid chromatography tandem mass spectometry method.

Study objective

In this observational trial we would like to study the possible correlation between the probe-drug dextromethrophan and tamoxifen pharmacokinetics. In case a good correlation is available, this might help in a stepwise development of truly individualizing tamoxifen treatment.

Study design

1. Day -28/-1: informed consent;

2. Day 1: pharmaokinetic sampling (pre, 30 min-24hours in total 9 sampling time points).

Intervention

Observational study with pharmacokinetic sampling.

Contacts

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Eligibility criteria

Inclusion criteria

1. Histological or cytological confirmed history of breast cancer for which treatment with tamoxifen monotherapy is indicated;

2. Age> or = 18 years;

3. WHO 0 or 1;

4. Adequate renal and hepatic functions;

5. Adequate hematological function;

6. Written informed consent;

7. Use of tamoxifen monotherapy for at least 3 weeks.

Exclusion criteria

1. Pregnant or lactating patients;

2. Patients with reproductive potential must use a reliable method of contraception;

3. Impossibility to take oral drugs;

4. Serious illness or medical unstable condition requiring treatment;

5. Symptomatic CNS-metastases or history of psychiatric disorder that would prohibit the understanding and giving of ijnformed consent;

6. Unwillingness to abstain form grapefruit (juice), (herbal) dietary supplements, herbals and over the counter medication (except paracetamol and ibuprofen) and other drugs known for to seriously interact with CYP3A and/or ABCB1 and/or ABCG2 during the study period;

7. Use of strong CYP3A and/or P-glycoprotein inhibiting and inducing medication, dietary supplements or other inhibiting compounds.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2009
Enrollment:	37
Type:	Anticipated

Ethics review

Positive opinion

Date:	31-03-2009
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL1653

Register	ID
NTR-old	NTR1751
Other	MEC : 09-YYY
ISRCTN	ISRCTN wordt niet meer aangevraagd

Study results

Summary results

de Graan et al. Dextromethorphan as a phenotyping test to predict endoxifen exposure in patients on tamoxifen treatment. J Clin Oncol. 2011;29(24):6240-6